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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
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GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
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(54) Title: REGULATION OF HUMAN TRANSIENT RECEPTOR POTENTIAL CHANNEL

(57) Abstract: Reagents which regulate human transient receptor potential channel and reagents which bind to human transient receptor potential channel gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, urinary incontinence, overactive bladder, benign prostatic hyperplasia, lower urinary tract syndromes, and CNS disorders.



WO 03/087158 A2

- 1 -

## SEQUENCE LISTING

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&lt;120&gt; Regulation of human transient receptor potential channel

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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&lt;213&gt; Homo sapiens

&lt;400&gt; 5

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&lt;400&gt; 6

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&lt;211&gt; 3639

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&lt;213&gt; Homo sapiens



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&lt;213&gt; Homo sapiens

&lt;400&gt; 8

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 9

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- 10 -

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<212> DNA
<213> Homo sapiens

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- 12 -

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 <211> 1095  
 <212> PRT  
 <213> Homo sapiens

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 35 40 45  
 Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
 50 55 60  
 Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
 65 70 75 80  
 Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
 85 90 95  
 Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110

- 13 -

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
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 His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140  
 Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160  
 Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175  
 Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190  
 Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
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 Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
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 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
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 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
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 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
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- 14 -

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
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 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
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 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
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 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
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 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
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 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
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 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
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 740 745 750  
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 755 760 765  
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 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
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 Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu  
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 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu  
 820 825 830

- 15 -

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 Phe Ala Val Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu  
 865 870 875 880  
 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr  
 885 890 895  
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly  
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 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
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 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
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 Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
 945 950 955 960  
 Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
 965 970 975  
 Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
 980 985 990  
 Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
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 <212> PRT  
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- 16 -

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 Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys  
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 Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly  
 100 105 110  
 Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile  
 115 120 125  
 Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu  
 130 135 140  
 Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg  
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 Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly  
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 Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile  
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 Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn  
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 Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp  
 210 215 220  
 Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr  
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 His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr  
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 Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg  
 275 280 285  
 Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe  
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 Ala Gln Gly Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile  
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 355 360 365  
 Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile  
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 405 410 415

- 17 -

Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn Gly Gln Leu Lys Leu  
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 Ala Leu Ile Lys Asp Arg Pro Lys Phe Val Arg Leu Phe Leu Glu Asn  
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 Gly Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu  
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 530 535 540  
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 Gly Val Gln Asn Phe Leu Ser Lys Gln Trp Tyr Gly Glu Ile Ser Arg  
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 Ala Tyr Val Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu  
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- 18 -

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 Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly Lys Lys  
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 Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu Val Ile  
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 Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg Met Arg  
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 Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly Ala Trp  
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 Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile Gly Glu  
 130 135 140  
 Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn Ile Val  
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 Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
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 Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
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- 20 -

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
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 Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110  
 Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
 115 120 125  
 His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140  
 Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160  
 Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175  
 Tyr Gly Leu Thr Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190  
 Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
 195 200 205  
 Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Ser Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380  
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445

- 21 -

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
 545 550 555 560  
 Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
 565 570 575  
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
 580 585 590  
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
 595 600 605  
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
 625 630 635 640  
 Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
 645 650 655  
 Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
 660 665 670  
 Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
 675 680 685  
 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
 690 695 700  
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
 705 710 715 720  
 Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
 725 730 735  
 Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
 740 745 750  
 Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val  
 755 760 765  
 Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
 770 775 780  
 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
 785 790 795 800

<400> 16  
Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
1 5 10 15

- 23 -

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
 20 25 30  
 Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
 35 40 45  
 Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
 50 55 60  
 Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
 65 70 75 80  
 Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
 85 90 95  
 Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110  
 Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
 115 120 125  
 His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140  
 Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160  
 Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175  
 Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190  
 Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
 195 200 205  
 Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380



- 24 -

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445  
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
 545 550 555 560  
 Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
 565 570 575  
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
 580 585 590  
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
 595 600 605  
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
 625 630 635 640  
 Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
 645 650 655  
 Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
 660 665 670  
 Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
 675 680 685  
 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
 690 695 700  
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
 705 710 715 720  
 Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
 725 730 735

- 25 -

Ile Ala Phe Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
 740 745 750  
 Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val  
 755 760 765  
 Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
 770 775 780  
 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
 785 790 795 800  
 Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu  
 805 810 815  
 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu  
 820 825 830  
 Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile  
 835 840 845  
 Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu  
 850 855 860  
 Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu  
 865 870 875 880  
 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr  
 885 890 895  
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly  
 900 905 910  
 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
 915 920 925  
 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
 930 935 940  
 Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
 945 950 955 960  
 Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
 965 970 975  
 Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
 980 985 990  
 Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
 995 1000 1005  
 Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys  
 1010 1015 1020  
 Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp  
 1025 1030 1035 1040  
 Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val  
 1045 1050 1055  
 Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg  
 1060 1065 1070  
 Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys  
 1075 1080 1085  
 Glu Ile Ala Asn Lys Ile Lys  
 1090 1095

- 26 -

<210> 17  
 <211> 652  
 <212> PRT  
 <213> Homo sapiens

<400> 17  
 Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
 1 5 10 15  
 Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
 20 25 30  
 Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
 35 40 45  
 Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
 50 55 60  
 Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
 65 70 75 80  
 Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
 85 90 95  
 Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110  
 Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
 115 120 125  
 His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140  
 Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160  
 Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175  
 Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190  
 Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
 195 200 205  
 Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320

- 27 -

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380  
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445  
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
 545 550 555 560  
 Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
 565 570 575  
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
 580 585 590  
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
 595 600 605  
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
 625 630 635 640  
 Ala Trp Gly Gly Leu Glu His His His His His His  
 645 650

<210> 18  
 <211> 1095  
 <212> PRT  
 <213> Homo sapiens

- 28 -

<400> 18  
 Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
 1 5 10 15  
 Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
 20 25 30  
 Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
 35 40 45  
 Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
 50 55 60  
 Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
 65 70 75 80  
 Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
 85 90 95  
 Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110  
 Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
 115 120 125  
 His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140  
 Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160  
 Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175  
 Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190  
 Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
 195 200 205  
 Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350

- 29 -

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380  
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445  
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
 545 550 555 560  
 Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
 565 570 575  
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
 580 585 590  
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
 595 600 605  
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
 625 630 635 640  
 Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
 645 650 655  
 Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
 660 665 670  
 Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
 675 680 685  
 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
 690 695 700  
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
 705 710 715 720

- 30 -

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
 725 730 735  
 Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
 740 745 750  
 Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val  
 755 760 765  
 Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
 770 775 780  
 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
 785 790 795 800  
 Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu  
 805 810 815  
 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu  
 820 825 830  
 Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile  
 835 840 845  
 Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu  
 850 855 860  
 Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu  
 865 870 875 880  
 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr  
 885 890 895  
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly  
 900 905 910  
 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
 915 920 925  
 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
 930 935 940  
 Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
 945 950 955 960  
 Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
 965 970 975  
 Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
 980 985 990  
 Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
 995 1000 1005  
 Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys  
 1010 1015 1020  
 Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp  
 1025 1030 1035 1040  
 Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val  
 1045 1050 1055  
 Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg  
 1060 1065 1070

- 31 -

Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys  
 1075 1080 1085

Glu Ile Ala Asn Lys Ile Lys  
 1090 1095

<210> 19  
 <211> 652  
 <212> PRT  
 <213> Homo sapiens

<400> 19  
 Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
 1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
 20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
 35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
 50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
 65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
 85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
 100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
 115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
 130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
 145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
 165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
 180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
 195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285



- 32 -

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380  
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445  
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
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-34-

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PCT

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C12Q 1/68, G01N 33/68, C07K 14/705

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(71) Applicant (for all designated States except US): **BAYER HEALTHCARE AG** [DE/DE]; 51368 Leverkusen (DE).

(72) Inventors; and

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(74) Common Representative: **BAYER HEALTHCARE AG**; Law and Patents, Patents and Licensing, 51368 Leverkusen (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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10 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: REGULATION OF HUMAN TRANSIENT RECEPTOR POTENTIAL CHANNEL

(57) Abstract: Reagents which regulate human transient receptor potential channel and reagents which bind to human transient receptor potential channel gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, urinary incontinence, overactive bladder, benign prostatic hyperplasia, lower urinary tract syndromes, and CNS disorders.

WO 2003/087158 A3



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03713

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/70 C12Q1/68 G01N33/68 C07K14/705

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 03/064602 A (NEUHAUSSER WERNER M ;JULIUS DAVID (US); MCKEMY DAVID D (US); UNIV) 7 August 2003 (2003-08-07) the whole document	1-8
P,X	WO 02/101045 A (IRM LLC ;NOVARTIS AG (CH); GANJU PAMPOSH (GB); BEVAN STUART (GB);) 19 December 2002 (2002-12-19) SEQ ID Nos 8 and 11	1-8
P,X	WO 02/087608 A (BOEHRINGER INGELHEIM PHARMA ;KRESS MICHAELA (DE); HABERBERGER RAIN) 7 November 2002 (2002-11-07) claims	1-8
P,X	WO 02/44210 A (SQUIBB BRISTOL MYERS CO (US)) 6 June 2002 (2002-06-06) claims 17-20,25	1-8
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

13 February 2004

Date of mailing of the international search report

15. 04. 2004

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
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Fax: (+31-70) 340-3016

Authorized officer

Routledge, B

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03713

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/10391 A (CURTIS RORY A J ;MILLENNIUM PHARM INC (US)) 7 February 2002 (2002-02-07) claims 17-26 -----	1-8
X	WO 02/10382 A (WISSENBACH ULRICH) 7 February 2002 (2002-02-07) claim 31 page 17, paragraph 6 - page 19, paragraph 1 -----	1-8
X	WO 02/04520 A (INCYTE GENOMICS INC) 17 January 2002 (2002-01-17) claims 19,20,22,23,25-27 -----	1-8
X	WO 02/02633 A (INCYTE GENOMICS INC ;TRIBOULEY CATHERINE M (US); RAUMANN BRIGITTE) 10 January 2002 (2002-01-10) claims 19,20,22,23,25-27 -----	1-8
X	WO 02/00722 A (SILOS SANTIAGO INMACULADA ;CURTIS RORY A J (US); MILLENNIUM PHARM) 3 January 2002 (2002-01-03) Seq ID No.5claim 2 page 137 - page 140 -----	1-8
X	WO 02/00718 A (SILOS SANTIAGO INMACULADA ;CURTIS RORY A J (US); MILLENNIUM PHARM) 3 January 2002 (2002-01-03) claims 17-35 page 2, line 34 - page 3, line 3 page 4, line 1 - line 29 -----	1-8
X	WO 01/077331 A (MILLENNIUM PHARMACEUTICALS INC ;SILOS SANTIAGO INMACULADA (US); CUR) 18 October 2001 (2001-10-18) claims 10-22,28-30 page 3, line 15 - line 25 page 7, line 1 - line 19 page 8, line 17 - line 23 -----	1-8
X	WO 01/068698 A (BOEHRINGER INGELHEIM) 20 September 2001 (2001-09-20) claims 43-57,68 page 28, line 25 - page 34, line 34 -----	1-8
X	WO 01/062794 A (LORA JOSE M ;CURTIS RORY A J (US); GLUCKSMANN MARIA ALEXANDRA (US)) 30 August 2001 (2001-08-30) claims 17-30,37,38 page 7, line 10 - line 21 page 12, line 17 - line 25 page 13, line 11 - line 16 -----	1-8
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03713

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/046258 A (INCYTE GENOMICS INC ;AZIMZAI YALDA (US); KHAN FARRAH A (US); REDDY) 28 June 2001 (2001-06-28) claims 19,20,22,23,25-27 -----	1-8
X	WO 00/40614 A (BETH ISRAEL HOSPITAL ;SCHARENBERG ANDREW M (US)) 13 July 2000 (2000-07-13) claims 24,36,37 -----	1-8
X	WO 00/04929 A (UNIV SOUTH ALABAMA) 3 February 2000 (2000-02-03) page 7, line 6 - line 12 page 15, line 12 - line 26 -----	1-8
X	WO 99/09140 A (BRAKE ANTHONY (US); JULIUS DAVID (US); UNIV.CALIFORNIA(US); CATERINA M) 25 February 1999 (1999-02-25) claim 19 -----	1-8

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/03713

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-8  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-8 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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Continuation of Box 1.2

Claims Nos.: 1-8

Given the breadth of the independent claims due to the definitions of the sequences which includes sequences of anything from 26% identity upwards, the initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to methods of screening using SEQ ID No.12.

Present claims 1-4 relate to an extremely large number of possible methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is not to be found, as the description merely represents a theoretical approach and does not exemplify the invention in practice. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely methods of screening using SEQ ID No.12.

Present claims 5-8 relate to a reagent and uses thereof defined by reference to a desirable characteristic or property, namely that the reagent has been identified using the screening methods of claims 1-4.

The claims cover all reagents having this characteristic or property, including known compounds (page 38 line 25) whereas the application provides does not provide support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for a single reagent as no specific reagents are identified. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound/method/apparatus by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of SEQ ID No.12.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Other documents relating to disclosure concerning transient receptor potential channels have also been added to the search report in order to illustrate the state of the art. However the list is not exhaustive and further documents may become relevant when the subject matter of the claims has been amended to overcome the above objections.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8 (partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.12 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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2. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.13 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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3. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.14 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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4. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.15 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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5. claims: 1-8 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.16 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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6. claims: 1-8 (partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.17 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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7. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.18 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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8. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.19 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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9. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.20 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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10. claims: 1-8(partially)



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.21 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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## 11. claims: 1-8 (partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.1 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 12. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.2 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 13. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.3 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 14. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.4 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 15. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.5 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 16. claims: 1-8(partially)

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.6 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 17. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.7 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 18. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.8 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 19. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.9 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 20. claims: 1-18(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.10 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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## 21. claims: 1-8 (partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.11 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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# INTERNATIONAL SEARCH REPORT

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International Application No

PCT/EP 03/03713

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